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Catheter-associated bloodstream infection incidence and risk factors in adults with cancer: a prospective cohort study

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SUMMARY

Central venous catheter-associated bloodstream infections (CABSIs) cause considerable morbidity in patients with cancer. We determined the incidence and risk factors for CABSI by performing a prospective observational cohort study of all adult patients requiring a central venous access device (CVAD) in a haematology–oncology unit. All CVADs were inserted under ultrasound guidance by trained operators in a dedicated interventional radiology facility. A total of 1127 CVADs were assessed in 727 patients over 51 514 line-days. The rate of CABSI per 1000 line-days was 2.50. Factors associated with CABSI included: type of CVAD, greatest for non-tunnelled lines [hazard ratio (HR): 3.50; $P < 0.0001$] and tunnelled lines (HR: 1.77; $P = 0.011$) compared to peripherally inserted central venous catheter (PICC) lines; patient diagnosis, greatest for aggressive haematological malignancies (HR: 3.17; $P = 0.0007$) and least for oesophageal, colon and rectal cancers (HR: 0.29; $P = 0.019$) compared to other solid tumours; side of insertion, greatest for right-sided lines (HR: 1.60; $P = 0.027$); and number of prior line insertions (HR: 1.20; $P = 0.022$). In patients with aggressive haematological malignancies there was significantly more CABSI with non-tunnelled lines (HR: 3.9; $P < 0.001$) and a trend to more CABSI with tunnelled lines (HR: 1.43; $P = 0.12$) compared to patients with PICC lines, as well as increased CABSI for right-sided insertions (HR: 1.62; $P = 0.047$). This study highlights the utility of a standardised CABSI surveillance strategy in adult patients with cancer, provides further data to support the use of PICC lines in such patient populations, and suggests that the side of line insertion may influence risk of CABSI.

Introduction

Central venous access devices (CVADs) are essential to the modern management of patients with haematological malignancies and solid tumours. An often serious complication is catheter-associated bloodstream infection (CABSI), which is a major cause of illness and mortality in patients with central lines. CABSI also contributes to increased costs of healthcare, primarily through increased duration of patient stay and greater treatment costs.[1,2] Haematology and oncology patients are particularly susceptible to infection because of their often compromised immune status and high burden of comorbidities. Identification of CABSI risk factors is important for optimising care of haematology–oncology patients with central lines and for risk adjustment in surveillance programmes.[3–5] The association between line type and risk of CABSI has been studied in detail, but relatively few studies have investigated other risk factors for CABSI in cancer patients, particularly in adults.[4]

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We conducted a prospective observational cohort study of adult patients in a haematology–oncology unit in a large tertiary hospital. The aims were to determine the incidence of CABSI using a robust line-day denominator, and to identify important risk factors for CABSI.

Methods

Study setting and population

This study was set in the Division of Cancer Services at the Princess Alexandra Hospital which is a tertiary referral centre in Brisbane, Australia. It includes haematology, medical oncology and radiation oncology units, and autologous but not allogeneic stem cell transplantation. All CVADs, whether elective or urgent insertions, were inserted by trained operators under ultrasound guidance in a dedicated interventional radiology facility within the Department of Radiology using aseptic techniques approved by the Infection Control Service.

The study population included adult patients of the Division of Cancer Services and included both inpatients and outpatients. All consecutive CVAD insertions between 1 January 2004 and 31 March 2007 were captured via the Division's CVAD database where prospective data on all CVAD insertions are collected. When an individual patient had more than one CVAD inserted during the study period, each was regarded as a separate event.

Following CVAD insertion, lines were managed according to a standardised Nursing Policy based on the Cancer Nurses Society of Australia CVAD Guidelines and USA Centres for Disease Control (CDC) Guidelines.[6,7] During the study period, antibiotic and antithrombotic prophylaxis were not routinely administered.

Definitions

CVAD was defined as any of the following: peripherally inserted central venous catheter (PICC); tunnelled central venous catheter (Catheter, Bard, Salt Lake City) non-tunnelled central venous catheter (MedComp®, DuoFlow catheter, MedComp, Harleysville); or implantable devices (e.g. Port-a-Cath®, Smith Medical, Kent). CVADs could be single, double or triple lumen. Peripheral venous catheters were excluded.

CABSI was defined according to the Australian Infection Control Association based on criteria from the National Nosocomial Infections Surveillance System from the CDC Atlanta, USA and from the Public Health Laboratory Service of the UK.[8–10] CABSIs were identified when: (a) the patient had a recognised pathogen isolated from one or more blood cultures (e.g. *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Escherichia coli*, *Klebsiella* spp., *Proteus* spp., *Candida albicans*); or (b) the patient had at least one of the following signs and symptoms within 24 h of a positive blood culture being collected (fever >38° C, chills, rigors, hypotension), and at least one of the following: isolation of a common skin commensal (e.g. diptheroids, coagulase-negative staphylococci, *Micrococcus* spp., *Propionibacterium* spp., *Bacillus* spp.) from two or more blood culture sets drawn on separate occasions within a 48 h period; or isolation of a common skin contaminant from a single blood culture and appropriate antimicrobial therapy is commenced. In addition to (a) and (b) above, the CVAD must have been present within 48 h of the event and the organism must not be related to an infection at another site. When first detected, all positive blood culture results were communicated by telephone to the treating physician by the laboratory staff and likely association with any intravenous line was documented. In the event of multiple episodes of positive cultures during the lifespan of a single CVAD, the first episode of CABSI was regarded as the single CABSI episode for the purposes of this study.

CABSI rate was defined as the number of CABSIs divided by the number of central line-days during the study period, multiplied by 1000.

Catheter-related bloodstream infection (CRBSI)[11] was defined as per CABSI but with additional isolation of the same organism from culture of the CVAD tip (roll tip method[12]) or growth of microbes from a blood sample drawn from a catheter hub at least 2 h before microbial growth was detected in a blood sample obtained from a peripheral vein (differential time to positivity criteria).[11]

Clinical suspicion of infection was defined when the decision to remove the CVAD was based upon clinical factors rather than a documented CABSI (e.g. fever persisting despite empiric antimicrobial therapy, isolation of organism from exit swab or blood culture results not meeting the definition of a CABSI).

Data and variables

Patient demographics and date of CVAD insertion were downloaded into the Cancer Services CVAD database each week. At the time of CVAD removal, medical or nursing staff entered additional data for that CVAD episode. Regular data quality checks were performed to update any missing variables.

Statistical analysis

The unit of analysis was a central line within a patient and the primary outcome was the number of line days until CABSI occurred. This was described using the Kaplan–Meier product limit method. Additionally, independent risk factors for CABSI were identified using a Cox proportional hazards regression model, constructed in SAS version 9.2 for Windows (SAS Institute, Cary, NC, USA). The proportional hazards assumption was checked for all variables included in these analyses. Initially, each variable was tested using univariate Cox regression models and only those variables with $P < 0.1$ were retained. A backwards elimination method was then used to remove variables from a multivariable Cox regression model, with variables excluded sequentially on the basis of Wald's *P*-value, until all remaining variables had $P \leq 0.05$. Goodness-of-fit of the final model was assessed using the concordance probability estimate.[13] A CPE of 0.5 implies a model that discriminates between shorter and longer times to infection no better than chance and a CPE of 1 discriminates perfectly. Robust sandwich estimates of variation were used in the regression analysis to take account of multiple lines within a patient. *P*-Values were not adjusted for multiple testing.

Secondary multivariate Cox regression analyses were performed for the outcomes: (i) CRBSI (tighter definition); (ii) line removal due to clinical suspicion of infection (looser definition); (iii) time to first CABSI infection within a patient.

Results

In total there were 1127 lines in 727 patients included in the analysis with 291 lines removed due to a clinical suspicion of infection; 129 of these were CABSI (of which 114 had a tip culture performed and 79 had sufficient cultures to be assessable for differential time to positivity criteria) and 54 met the definition of CRBSI. The number of days per inserted line ranged from <1 to 936, with a median of 29 and an overall total of 51 514 line days. The rate of CABSI per 1000 line-days was 2.5. The rates of other end-points per 1000 line-days were 5.65 for clinical suspicion of infection and 1.05 for CRBSI. The other variables collected on the patients are